

### AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A genetic construct (10) which is suitable for the an insertion/deletion and an inversion for at least one target nucleotide sequence (A) ~~and comprised of either comprising:~~

- a promoter/activator sequence (11) disposed upstream of a first ~~and a second~~ nucleotide sequence (1,2) encoding ~~two different a first toxic molecules-molecule and a second nucleotide sequence encoding a second toxic molecule different from said first toxic molecule,~~ or

- a first promoter/activator sequence (11) disposed upstream of a ~~the~~ first nucleotide sequence (1) encoding a first toxic molecule and disposed in the an opposite direction of said first nucleotide sequence, and a second promoter/activator sequence (12) disposed upstream of a second nucleotide sequence encoding an antidote (2') to a second toxic molecule different from said first toxic molecule, or

- a promoter/activator sequence (11) disposed upstream of a first nucleotide sequence encoding the first toxic molecule and a second nucleotide sequence (1,2') encoding ~~respectively a first toxic molecule and an antidote to a~~ the second toxic molecule different from said first toxic molecule.

2. **(Currently amended)** The genetic construct (10) according to claim 1 suitable for the inversion of at least one target nucleotide sequence (A) and comprised of

- a first promoter/activator sequence (11) disposed upstream, of a first nucleotide sequence ~~(1) encoding a the~~ toxic molecule, ~~and~~

- a second nucleotide sequence (2') encoding an antidote to a second toxic molecule different from said first toxic molecule wherein the second nucleotide sequence is and, ~~disposed in the an~~ opposite direction to the lecture-reading orientation of the first promoter/activator sequence (11), ~~preferably under the control of a second promoter/activator sequence (12) and,~~

- a third nucleotide sequence (1') encoding an antidote to said first toxic molecule.

3. **(Currently amended)** ~~A nucleic acid~~ The genetic construct according to claim 1 ~~or 2,~~ wherein each nucleotide sequence (1,2,1',2') encoding a toxic molecule or an antidote to a toxic molecule is a nucleic acid sequence which encodes a fusion protein active as a toxic molecule or as an antidote to said toxic molecule, said nucleic acid sequence which encodes said

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fusion protein ~~being made of comprising~~ a coding nucleotide sequence which comprises several unique cloning sites and a nucleotide sequence encoding a ~~toxic molecule~~ toxic to a cell or an antidote to ~~a said~~ a toxic molecule.

4. **(Currently amended)** The genetic construct (10) according to Claim 1 ~~any of the preceding claims~~, which further comprises recombination sites disposed upstream and downstream the nucleotide sequence(s) (1, 2) encoding ~~a the first and the second~~ the first and the second ~~toxic molecule~~ toxic molecules and/or the nucleotide sequence(s) (1', 2') encoding an antidote to a toxic molecule.

5. **(Currently amended)** The genetic construct (10) according to Claim 1 ~~any of the preceding claims~~, wherein the sequences (1, 2, 1', 2') encoding the toxic molecule and the antidote to the toxic molecule are poison/antidote sequences, ~~preferably selected from the group consisting of the following poison/antidote systems: CcdB/CcdA, Kid/Kis, Hok/Sok, Doc/Phd, RelE/RelB, PasA/PasB/PasC, MazE/MazF, ParE/ParD.~~

6. **(Currently amended)** A cloning vector comprising at least one of the genetic construct (10) according to Claim ~~any of the preceding claims 1 to 5~~.

7. **(Currently amended)** The cloning vector according to claim 6 further comprising an origin of replication and a selectable marker, ~~preferably an antibiotic resistance selectable marker.~~

8. **(Currently amended)** A cell transformed by the genetic construct ~~according to of Claim any of the preceding claims 1 to 5 or the vector according to any of the preceding claims 6 to 7 or comprising integrated in its chromosomal genome at least one genetic construct according to any of the preceding claims 1 to 5.~~

9. **(Currently amended)** The cell according to claim 8 which is selected from the group consisting of prokaryote cells, plant cells, animal cells ~~(including human cells)~~ and fungi cells ~~(including yeast cells).~~

10. **(Currently amended)** A cloning and selection kit comprising an element selected from the group consisting of one or more nucleic acid construct according to ~~any of the preceding claims Claim 1 to 5~~, one or more vectors comprising at least one genetic construct of Claim 1 ~~according to the claim 6 or 7~~ and cells to be transformed by said construct or vector, wherein said cells ~~which~~ are either resistant or sensitive to one or more of said toxic molecule(s), or wherein said cells are expressing one or more of said toxic molecule(s) or antidote(s) to said toxic molecule(s).

11. **(Currently amended)** A method for an insertion and ~~possibly a deletion~~ and/or an inversion of a target nucleotide sequence (A) into a nucleic acid construct ~~and said method~~ comprising the following steps, ~~preferably performed by an automate:~~

- ~~- possibly selecting said target nucleotide sequence from genome databases through analysis of said genomic sequence by the identification of exon-intron structure and comparison with expression genetic databases,~~
- ~~- possibly providing primer sequences suitable for a genetic amplification and cloning of said target genetic sequence,~~
- ~~- possibly selecting elements of said nucleic acid construct presented in databases as well as cells to be transformed by said nucleic acid construct,~~
- ~~- possibly providing the design of the nucleic acid construct suitable for the integration of said target nucleotide sequence and possibly recovering the design of the obtained virtual nucleic acid construct into a target memory database,~~
- providing ~~(possibly from said design)~~ a nucleic acid construct according to any of the preceding claims Claim 1 to 5, ~~possibly integrated into the vector of the claim 6 or 7 or in the cell according to the claim 8 or 9~~ and obtaining the insertion of said target nucleotide sequence into the nucleic acid construct by inactivation of a nucleotide sequence encoding a toxic molecule and
- selecting the nucleic acid construct having integrated said target nucleotide sequence in a cell which is ~~sensible~~ sensitive to said toxic molecule.

12. **(Currently amended)** The method according to claim 11 which further comprises the step of ~~the replacement of~~ replacing the target nucleotide sequence by the elements which have been deleted following the insertion of said target nucleotide sequence or by the integration of a target nucleotide sequence having an inverted ~~lecture~~ reading orientation.

13. **(Currently amended)** The method according to ~~the claim 11 or 12~~, wherein said integration of the target nucleotide sequence, replacement or inversion of the target nucleotide sequence is a step selected from the group consisting of ~~obtained by classical~~ restriction/ligation, site specific recombination, TOPO cloning and homologous recombination.

14. **(Currently amended)** The method according to Claim ~~any of the preceding claims 11 to 13~~, which comprises the step of insertion/deletion and/or reversion of several target nucleotide sequences (A, B, C, D, E, F) into multiple nucleic acid construct(s) and the step of

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selecting simultaneously ~~preferably in a single cell or in a single reaction tube, the~~ a construct having integrated, deleted or inverted ~~correctly~~ said target nucleotide sequences.

15. **(Currently amended)** A computer ~~Computer~~ program comprising program codes means for performing the steps according to Claim ~~any of the preceding claims 11 to 14.~~

16. A computer ~~Computer~~ program ~~products-product~~ comprising the program codes means on a computer readable medium for performing the steps of the method according to Claim ~~any of the preceding claims 11 to 13~~ when said program is run on a computer.

17. **(Currently amended)** An automate connected to a database of a computer and which comprises an element selected from the group consisting of the nucleic acid genetic construct according to Claim ~~the claims 1 to 5 or, the~~ a vector comprising at least one genetic construct of Claim 1, according to the claims 6 to 7 or the cells and a cell transformed by the genetic construct of Claim 1 according to the claims 8 to 9 or the elements of the kit according to the claim 10 and possibly the computer program of claim 15 or 16, for performing the method according to any of the preceding claims 11 to 13.

18. **(New)** The genetic construct of Claim 2, wherein said second nucleotide sequence encoding said antidote to said second toxic molecule is under the control of a second promoter/activator sequence.

19. **(New)** The genetic construct according to the claim 5, wherein the poison/antidote sequences are selected from the group consisting of the following poison/antidote systems: CcdB/CcdA, Kid/Kis, Hok/Sok, Doc/Phd, RelE/RelB, PasA/PasB/PasC, MazE/MazF and ParE/ParD.

20. **(New)** The vector of claim 7, wherein the selectable marker is an antibiotic resistance selectable marker.

21. **(New)** The cell of Claim 9, wherein said animal cells are human cells.

22. **(New)** The cell of Claim 9, wherein said fungi cells are yeast cells.

23. **(New)** The method of claim 11 further comprising:

- selecting the target nucleotide sequence from genome databases through analysis of a corresponding genomic sequence by identification of exon-intron-structure and comparison with expression genetic databases,

- providing primer sequences suitable for a genetic amplification and cloning of said target genetic sequence,

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- selecting elements of the nucleic acid construct presented in databases as well as cells to be transformed by the nucleic acid construct, and

- providing a design of the nucleic acid construct suitable for an integration of the target nucleotide sequence.

24. (New) The method according to claim 14, wherein the step of selecting simultaneously a construct having integrated, deleted or inverted the target nucleotide sequences is made in a single cell or in a single reaction tube.